ESO-KAROLINSKA STROKE UPDATE
Conference | Stockholm | November 16-18 | 2014

Consensus statement on mechanical thrombectomy in acute ischemic stroke

A collaboration of the ESO – Karolinska Stroke Update, ESMINT and ESNR

European Stroke Organisation (ESO)

European Society for Minimally Invasive Neurological Therapy (ESMINT)

European Society of Neuroradiology (ESNR)

Please note that this is not a formal ESO guidelines, but a consensus statement. As soon as the guidelines in collaboration with ESMINT, ESNR and other European societies are completed, they will appear on the ESO-Karolinska website as well as on the different societies' websites.

Consensus statement on mechanical thrombectomy in acute ischemic stroke – ESO-Karolinska Stroke Update 2014 in collaboration with ESMINT and ESNR

New evidence since KSU 2012

Since the previous Karolinska Stroke Update consensus statement on mechanical thrombectomy 2012, results from randomized clinical trials and other retrospective cohort studies were made available as follows:

A. Large metaanalysis from randomized clinical trials of intravenous thrombolysis (IVT)

A recently published meta-analysis of individual patient data from 6756 patients in nine randomized trials comparing IVT with alteplase versus placebo or open control showed that alteplase significantly improves functional outcomes when delivered within 4,5 h of stroke onset, with earlier treatment associated with bigger proportional benefits (OR 1·75, 95% CI 1·35–2·27), thus emphasizing the need for preventing delays in acute stroke treatment.[1]

B. Randomized clinical trials on mechanical thrombectomy

a) Older generation devices and first use of stent retrievers

Three trials evaluating endovascular therapy, published in 2013, IMS III, MR RESCUE and SYNTHESIS, reported neutral results on clinical outcome. Possible explanations for failure to demonstrate superiority of endovascular therapy were long delay between symptom onset and treatment, inadequate patient selection, less than desired recanalization rates and use of older generation devices. IMS III showed no difference in safety and clinical outcomes compared to IVT but used 6 different procedural techniques with only 4 patients being treated with the new generation stent retrievers.[2] A subgroup analysis of IMS III showed 48.2% modified Rankin score (mRS) 0-2 when recanalization mTICI 2b/3 was achieved (for ICA (37-42%) and M1 occlusions (44%))[3], emphasizing the importance of recanalization of proximal occlusion. Importantly, IMS III demonstrated that a delay in time to reperfusion was associated with lower likelihood of good clinical outcome.[4] MR RESCUE allowed procedures up to 8 h based on penumbral imaging but used previous generation MERCI or Penumbra devices achieving mTICI 2b/3 recanalization rates of 67%.[5] The SYNTHESIS EXPANSION trial also used very few stent retrievers.[6] However, regarding safety, these trials showed similar rates of symptomatic intracranial hemorrhage (SICH) compared to IVT and even equivalence/superiority of IVT for minor stroke and stroke without large vessel occlusion on imaging.[7]

b) Stent retrievers in recent randomized controlled trials

Two smaller phase IIb randomized controlled studies compared stent retrievers with the original MERCI™ device (see also thrombectomy consensus statement from the 2012 KSU meeting).

The **SWIFT** study (Solitaire™ With the Intention For Thrombectomy) compared thrombectomy with the Solitaire™ and with the MERCI™ devices and was prematurely stopped after 113 patients because of efficacy. The primary outcome, recanalisation defined as Thrombolysis In Myocardial Ischemia (TIMI) scale 2 or 3, was more frequent with the Solitaire ™ device with an odds ratio (OR) of 4.9 (95% CI 2.1–11.1). Also, 3 months mRS ≤ 2 was more frequent with the Solitaire™ with an OR of 2.8 [1.2–6.2].[8]

The **TREVO-2** trial (Trevo versus Merci retrievers for thrombectomy REvascularisation of large Vessel Occlusions) compared thrombectomy with the TREVO Retriever™ and with the MERCI™ device in 178 patients. Reperfusion measured by Thrombolysis In Cerebral Infarction (TICI) scores of ≥ 2 was more frequent with the TREVO Retriever™ with an OR of 4.2 (95% CI 1.9–9.7). 3 months mRS ≤ 2 was more frequent with Trevo™: 40.0% vs. 21.8%, but there was a trend towards higher mortality.[9]

The **MR CLEAN** trial (Multicenter Randomized Clinical trial of Endovascular Treatment in the Netherlands)[10], using stent retrievers in 97% of the cases, showed benefit of endovascular therapy up to 6 h after stroke onset in the proximal anterior circulation in addition to best medical therapy (IVT up to 4.5 h in most patients). Onset to IVT was 85-87 min in both intervention and control groups and onset time to arterial puncture was 260 min. The endovascular procedure was associated with a shift to improved function at 90 days, as reflected in more patients in the lower mRS categories, with an adjusted common odds ratio (acOR) of 1.67 (95% confidence interval [CI], 1.21 - 2.30).

Secondary outcome parameters (NIHSS at 24h and 1wk, recanalization at 24h and final infarct at 1wk) were all statistical significantly favoring the intervention group. Treatment effect was consistent in all pre-defined subgroups.

The **ESCAPE** trial (Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times) was prematurely halted after randomization of 316 patients due to a positive interim analysis. To be randomized, patients needed to have a NIHSS > 5, a CTA confirmed occlusion of the carotid T or the middle cerebral artery (MCA, M1 or large M2 segment), good collaterals on multiphase CTA, a CT-ASPECTS > 5, and had to be enrolled < 12 hours. rtPA before randomization was given if patients were eligible. *Results*: The adjusted risk ratio for a mRS shift with thrombectomy at 90 days was 3.1 (CI : 2.0 – 4.7). A favourable modified Rankin *score* (mRS) of 0-2 at 90 days was seen in 53.0% in thrombectomy vs. 29.3% in controls (NNT=4), and reduction of mortality was significant. All subgroups of patients had similar benefit, including the elderly and patients treatable after 6 hours from onset time. About 75% of patients received IVT and stent retrievers were used in 86.1%.[11]

The **SWIFT PRIME** trial (Solitaire™ With the Intention For Thrombectomy as PRIMary treatment for acute ischemic strokE) was prematurely stopped after a positive interim analysis of the first 196 patients. To be randomized, all patients needed to have received IVT < 4.5 hours, a NIHSS between 8 and 29, a CTA or MRA showing an occlusion of the intracranial carotid or M1 segment of the MCA without extracranial carotid occlusion, an ASPECTS > 6 and CT hypodensity (or MRI hyperintensity) < 1/3 of the MCA territory, and treatable < 6 hours. *Results* (two co-primary endpoints): The OR for a mRS shift at 90 days with thrombectomy using the Solitaire™ FR stent retriever was highly significant (p< 0.001), and mRS 0-2 at 90 days was 60.2% in thrombectomy patients vs. 35.5% in controls (p < 0.001, NNT=4). There was a trend for reduced mortality. The onset-to-arterial-puncture delay was 252 min. All subgroups of patients had similar benefit.[12]

The **EXTEND-IA** trial (EXtending the time for Thrombolysis in Emergency Neurological Deficits with Intra-Arterial therapy), a phase II trial looking at early reperfusion and neurological improvement on day 3, was prematurely stopped because of a positive interim analysis of the first 70 randomized patients. To be randomized, all patients needed to have received IVT < 4.5 hours, a CT or MR angiography showing an occlusion of the intracranial carotid, M1 or M2 segment of the MCA, significant mismatch and limited core on MR- or CT perfusion (using the RAPID® software), and had to be treatable <6 hours. *Results* (two co-primary endpoints): Early reperfusion of the ischemic tissue at 24h hours with thrombectomy with the Solitaire™ FR stent retriever was 100% vs. 37% in the control group (p<0.001), a NIHSS reduction ≥ 8 points or NIHSS 0-1 at 3 days with thrombectomy was 80% vs 37% in the control group (p<0.001). mRS 0-2 at 90 days was 71% in thrombectomy patients and 40% in controls (p<0.01, NNT =3). There was a trend towards reduction of mortality. The onset-to-arterial-puncture delay was 210 min.[13]

In summary, there is very good evidence for early thrombectomy with stentretrievers. There is good evidence to favour stentretrievers over the MERCI™ device. At this moment only limited data on other types of recanalization devices such as the Penumbra™ system are available.[14] Given the variable success rates and clinical outcomes with different recanalisation devices in randomized trials, generalizability of all transvascular approaches cannot be assumed.

C. Aspects to be considered in mechanical thrombectomy

a) Stent retrievers

The STAR (Solitaire Flow Restoration Thrombectomy for Acute Revascularization) study was an international, multicentre, prospective, single-arm study of the Solitaire™ device in 202 patients with large vessel occlusion of the anterior circulation within 8 h of onset. It reported a 79% rate of successful revascularization, 57.9% of mRS 0-2, 1.5% SICH and 6.9% mortality. Support for stent retrievers was further gathered in a 2013 pooled analysis of 19 studies using the Trevo™ (n=221) or Solitaire™ (n=355) devices, showing mTICI 2b-3 scores in 83 and 82%, hemorrhage in 8 and 6%, device complications in 5 and 6%, good functional outcomes in 51 and 47% of the patients with similar times to recanalization and with a mortality of 31 and 14%, respectively.[15]

b) Mechanical thrombectomy in single centre cohorts: outcomes and risk factors

A recently published single centre series of 240 patients treated 2005-2011 with mechanical thrombectomy alone or in addition to IVT (40%) (using initially MERCI™ and later on stentretrievers) achieved 50% mRS 0-2 at 3 months and reported 4.6% of SICH.[16]

In a retrospective single centre cohort of 176 consecutive patients focusing on complications of mechanical thrombectomy it was shown that prolonged endovascular procedure beyond one hour was associated with higher complication rates (such as SICH, embolism to new territories, dissection, vasospasm, stent dislocation/occlusion, cumulative 11% rate) but that the overall rate of SICH (5%) was comparable to IVT.[17] Postinterventional subarachnoid hyperdensities were not shown to influence outcomes.[18]

c) Mechanical thrombectomy in elderly patients

In MR CLEAN 16% of the patients were 80 years or older; there was a positive treatment effect in this subgroup. This effect was significant and its size not different from the main effect size (OR 3.24, 95% CI 1.21-8.62)[10]. Similarly, both randomized trials ESCAPE and SWIFT PRIME (in the latter with upper age limit of 80 years old) showed benefit for all subgroups including the elderly, who should thus be considered for thrombectomy.[11, 12] Previously, mortality in patients undergoing thrombectomy over 80 years of age was reported to be double that for younger patients in a large multicentre retrospective analysis in the US (9300 patients, of which 18% were above 80). However, the analysis period was restricted to 2008-2010, the type of device used was not mentioned and treatment effect could not be asessed.[19] Almekhlafi et al. used the SPAN-100 index (i.e. positive index if age+NIHSS score = 100 or more) and found lower proportions of favourable outcome in the patients with positive (61%) compared to negative SPAN index (27%, OR 0.3; 95% CI 0.1-0.9), with 60% of positive SPAN index being 80 years of age and older.[20] For the vertebrobasilar circulation, a retrospective analysis from a US nationwide database from 2006-2010 showed that age had an impact on in-hospital mortality of patients undergoing mechanical thrombectomy (n=631) but not IVT (n=1554), in particular those 65 years of age or older (43 vs 23%). However, the types of devices used during that period were not reported.[21]

d) Time to treatment and reperfusion

The positive effect in the MR CLEAN trial was time-dependent, with acOR decreasing from 3.0 (95% CI: 1.6 – 5.6) at 3.5 hours onset to reperfusion time, to 1.5 (95% CI: 1.1 – 2.2) at 6 hours.[22] Treatment effect was not statistically significant anymore when reperfusion was achieved after 6h19m.
Benefit of thrombectomy was also shown to be time-dependent in IMS III, where increased time to reperfusion was associated with a decreased probability of good functional outcome (adjusted relative risk for every 30-min delay 0·88, 95% CI 0·80-0·98).[4] Based on IMS III results and literature review, a cutoff of 347 min (5h47m) for superiority of endovascular procedure over IVT alone was recently suggested.[23] These findings underline the necessity to treat as early as possible, and justify the time window of treatment within 6 hours from symptom onset.

In the ESCAPE trial, however, 49 (15.5%) patients were included beyond 6 hours, treatment effect was not different. This leaves room to investigate the possibilities of expanding the treatment time window for a selected group based on advanced imaging.

e) Tandem pathology

In the MR CLEAN trial 146 (29%) patients had an additional extracranial ICA occlusion (tandem pathology), with treatment effect in favor of thrombectomy (OR 1.43, 95% CI 0.78-2.64).[10]

In a systematic review of 32 studies including 1107 patients with intra and/or extracranial ICA occlusions, intraarterial thrombolysis was compared with any kind of mechanical treatment and/or stent placement. Acute stenting of occlusions of the extracranial ICA resulted in a higher recanalization rate (87% vs 48%, p=0.001) and favorable outcomes (68% vs 15%, p<0.001) as well as lower mortality (18% vs 41%, p=0.048) when compared to intra-arterial thrombolysis[24].

Recently published cohort studies indicate that tandem stenosis/occlusions of the ICA/MCA can be treated with acute stenting of the extracranial internal carotid and stent retriever mechanical thrombectomy in the MCA with a reasonable risk profile.[25-29] However further evaluation of this treatment strategy is warranted.

f) Basilar artery occlusion

Despite high mortality and morbidity rates associated with basilar artery occlusion [30], evidence from RCT's is lacking. A recent meta-analysis of 45 studies (n=2056) of reperfusion of acute basilar occlusion showed numbers needed to treat (NNT) of 3 and 2.5 to decrease death or dependency and death alone, respectively.[31]

Single-centre studies with samples inferior to 100 patients have shown good functional outcomes following thrombectomy of the basilar artery ranging from 30% [32, 33] to 48%. [34-36] Experience at the Karolinska Hospital showed a 57% rate of good functional outcome (95% CI 37% to 75%), and of 73% (95% CI 50% to 89%) when there were no signs of acute infarction prior to treatment, with about 21% mortality.[37]

Recanalisation rates over 75% were reported with new generation devices [33, 38] as well as with older generation devices in the MERCI and multi-MERCI trials but with lower benefit.[39]

A previous prospective registry, the Basilar Artery International Cooperation Study (BASICS) could not demonstrate superiority of endovascular therapy against IVT, however, it employed mostly older-generation devices.[40] The same investigators are now undertaking the BASICS treatment trial, comparing thrombectomy <6 hours in addition to IVT with IVT alone.

g) Anesthesia in mechanical thrombectomy

Conscious sedation has gained support from a retrospective analysis of patients receiving either general anesthesia or conscious sedation (n= 507 in both groups, 1:1 matching). Patients receiving general anesthesia had significantly more in-hospital mortality (25%) and pneumonia (17%) compared to patients receiving conscious sedation (12% and 9.3%, OR 2.37 and 2.0, respectively), but similar rates of SICH.[41] A recent mini review from Takahashi et al also supports conscious sedation[42]. Previous single-centre cohort studies [43, 44] and a review of 5 such studies [45] have reported similar findings. The post-hoc analysis of the thromboectomy patients in MR CLEAN showed better functional 3 months outcome in the absence of general anesthesia, but patients were not randomized to the type of anesthesia.[46]

An expert consensus statement of the Society of Neurointerventional Surgery and the Neurocritical Care Society recommends the use of general anesthesia for patients with severe agitation, low level of consciousness (GCS <8), loss of airway protective reflexes, respiratory compromise and in selected posterior circulation stroke presenting with these features.[47]

h) Prehospital patient selection for immediate transfer to centres with multimodal imaging and availability of thrombectomy

A recently published SITS registry study found NIHSS scores of 11 and 12 points as predictors of baseline vessel occlusion and functional independence at 3 months in a cohort of 11,632 patients with available baseline imaging data and 3 month functional outcome.[48] Moreover, if imaging was performed 3 h after stroke onset, NIHSS scores thresholds decreased to 9 and 10 points in predicting baseline vessel occlusion and functional outcome at 3 months, respectively. These results are in line with an initial single-centre retrospective study of 162 patients showing that a NIHSS score of 10 or more points up to 6 h after stroke onset increased by 16.9-fold the odds of unfavourable outcome or death ($p = 0.013$), and by 7.13-fold the odds of proximal vessel occlusion ($p = 0.013$ and $p < 0.038$, respectively; sensitivity, 83%; specificity, 78%).[49]

i) Imaging-guided patient selection

Acute non-invasive arterial imaging: All recent RCT trials of thrombectomy used non-invasive arterial imaging (CT-angiograhy or MR-angiography of cerebral and neck arteries) to select patients with an intracranial occlusion of the distal carotid and/or middle cerebral artery or M2 main stem. This may be a reason why such trials were positive, in contrast to the previous thrombectomy trials. If non-invasive arterial imaging cannot be performed, an elevated NIHSS ≥ 9 points within the first 3 hours, and ≥ 7 between 3 and 6 hours strongly suggests an occlusion of a major intracranial artery.[48, 50] Still, acute non-invasive imaging of cervical and intracranial arteries is clearly superior to identify the appropriate patients for acute mechanical thrombectomy and should be performed for all patients who have clinical criteria for thrombectomy, and no contraindication to such added imaging.

ASPECTS (Alberta Score Program Early CT Score) on plain CT. The MR CLEAN trial subgroup analysis showed benefit of thrombectomy for patients with ASPECTS scores of 5 or more points (5-7 points, OR 1.97 and 8-10 points, OR 1.61, respectively) but probably not with ASPECTS scores 0-4 (OR 1.09, large 95% CI 0.14-8.46). Higher baseline ASPECTS also predicted favourable outcome in a cohort of 202 patients treated with Solitaire FR [20] and in a cohort 149 patients treated with Solitaire and Penumbra aspiration system[51] The MR RESCUE study, in which the penumbra was identified with multimodal CT or MRI for patient randomization, showed neutral results for mechanical thrombectomy. In the ESCAPE and SWIFT-PRIME trials, a lower ASPECTS threshold of 5 and 6 were applied, respectively. Above these values, thrombectomy showed similar efficacy for different ASPECTS scores.[11, 12]

MRI-based imaging: DWI, PWI, mismatch: The single-centre RECOST study using MRI DWI-derived ASPECTS score on 165 patients showed benefit of thrombectomy when using this imaging technique for patient selection where the elderly could benefit from stent retriever thrombectomy if the ischemic core volume was low (with a clear cutoff at 70 years-old) whereas all patients below 70 years of age could benefit.[52] A smaller study from the same centre on 31 consecutive patients, focusing on basilar artery occlusion treated with Solitaire FR device, found a good correlation between brainstem DWI score < 3 and favourable clinical outcome.[36] The prospective, single-arm multicentric DEFUSE-2 trial showed favourable clinical outcomes in patients selected for endovascular treatment with MRI PWI mismatch in MCA or ICA occlusions (n=98, about half pretreated with IVT).[53]

Perfusion-CT based imaging: A multicentre analysis of 165 patients, the vast majority of whom underwent endovascular or intravenous recanalisation treatment, showed independent prognostic value of core and penumbra volumes on clinical outcome.[54] The importance of recanalisation was particularly striking in patients with large penumbra volumes.[55] In the positive EXTEND-IA trial, patients were selected based on a CTP showing a mismatch ratio >1.2, and absolute mismatch volume >10 ml, and an ischemic core lesion volume <70 ml, using RAPID™ software.[13]

D. Discussion regarding ongoing and future studies on mechanical thrombectomy

The recent results from several randomized controlled studies could potentially influence patient recruitment in ongoing RCT's such as PISTE or BASICS. Until steering committees of the respective trials have halted the trial, randomization should be continue to help answer uncertainties of benefit and risk from thrombectomy in acute ischemic stroke.

Studies comparing active centres (IVT + possibility for thrombectomy) with control centres who do not yet have access to thrombectomy (IVT treatment alone), e.g. SITS-OPEN, should continue its recruitment to strengthen the level of evidence. There are many reasons to recommend this approach such as the need for confirmatory studies, the desirability of narrowing the confidence interval to get a tighter estimate of the effect size for health economic reasons and the necessity for a wide range of data allowing subgroup analysis with adequate power. This type of design will also test thrombectomy in standard clinical practice in experienced centres.

In addition, it is desirable that all patients undergoing some form of acute revascularization therapy (IVT, mechanical thrombectomy, etc.) are prospectively included in registries (e.g. SITS or SITS-TBY) to ensure further evidence from routine clinical practice data.

Consensus statements of the ESO-Karolinska Stroke Update, in collaboration with ESMINT and ESNR

Prepared in December 2014, updated and released on February 20th 2015, after the International Stroke Conference

(Sources: Oxford Evidence-based level of evidence, Karolinska Stroke Update level of evidence for treatment recommendation)

Treatment recommendations

- Mechanical thrombectomy, in addition to intravenous thrombolysis within 4.5 hours when eligible, is recommended to treat acute stroke patients with large artery occlusions in the anterior circulation up to 6 hours after symptom onset (Grade A, Level 1a, KSU Grade A). - *new*
- Mechanical thrombectomy should not prevent the initiation of intravenous thrombolysis where this is indicated, and intravenous thrombolysis should not delay mechanical thrombectomy (Grade A, Level 1a, KSU Grade A). - *changed*
- Mechanical thrombectomy should be performed as soon as possible after its indication (Grade A, Level 1a, KSU Grade A).
- For mechanical thrombectomy, stent retrievers approved by local health authorities should be considered (Grade A, Level 1a, KSU Grade A). - *new*
- Other thrombectomy or aspiration devices approved by local health authorities may be used upon the neurointerventionists discretion if rapid, complete and safe revascularisation of the target vessel can be achieved (Grade C, Level 2a, KSU Grade C) - *new*
- If intravenous thrombolysis is contraindicated (e.g. Warfarin-treated with therapeutic INR) mechanical thrombectomy is recommended as first-line treatment in large vessel occlusions (Grade A, Level 1a, KSU Grade A) – *changed and updated level of evidence*.
- Patients with acute basilar artery occlusion should be evaluated in centres with multimodal imaging and treated with mechanical thrombectomy in addition to intravenous thrombolysis when indicated (Grade B, Level 2a, KSU Grade C); alternatively they may be treated within a randomized controlled trial for thrombectomy approved by the local ethical committee - *new*
- The decision to undertake mechanical thrombectomy should be made jointly by a multidisciplinary team comprising at least a stroke physician and a neurointerventionalist and performed in experienced centres providing comprehensive stroke care and expertise in neuroanesthesiology (Grade C, Level 5, GCP, KSU Grade C).
- Mechanical thrombectomy should be performed by a trained and experienced neurointerventionalist who meets national and/or international requirements (Grade B, Level 2b, KSU Grade B) – *changed in level of evidence*.
- The choice of anesthesia depends on the individual situation; independently of the method chosen, all efforts should be made to avoid thrombectomy delays (Grade C, Level 2b, KSU Grade C) – *changed.*

Patient selection

- Intracranial vessel occlusion must be diagnosed with non-invasive imaging whenever possible before considering treatment with mechanical thrombectomy (Grade A, Level 1a, KSU Grade A) - *new*.
- If vessel imaging is not available at baseline, a NIHSS score of ≥ 9 within three, and ≥ 7 points within six hours may indicate the presence of large vessel occlusion (Grade B, Level 2a, KSU Grade B) - *new*.
- Patients with radiological signs of large infarcts (for ex. using the ASPECTS score) may be unsuitable for thrombectomy (Grade B, Level 2a, KSU Grade B) - *new*

- Imaging techniques for determining infarct and penumbra sizes can be used for patient selection and correlate with functional outcome after mechanical thrombectomy (Grade B, Level 1b, KSU Grade B) - *new*.
- High age alone is not a reason to withhold mechanical thrombectomy as an adjunctive treatment (Grade A, Level 1a, KSU Grade A) - *new*.

Recommendation for implementation, registries and further trials

- Health authorities are strongly encouraged to implement access to thrombectomy within a reasonable time range in a network including stroke centres - *new.*
- It is encouraged to perform and include patients in RCT addressing unresolved thrombectomy questions such as thrombectomy for basilar artery occlusion, treatment in a late und unknown time windows, treating patients with imaging findings not sufficiently covered in recent trials, comparing new devices with widely-used stent retrievers, thrombectomy with or without intravenous thrombolysis, and different types of anesthesia*. - new.*
- Non-randomized trials comparing centres not yet having access to mechanical thrombectomy with others should continue (such as SITS OPEN) - *new.*
- Ischemic stroke patients undergoing any type of acute revascularization treatment should be included systematically in national or international registries (such as SITS or SITS-TBY) - *new.*

References

1. Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: A meta-analysis of individual patient data from randomised trials. *Lancet*. 2014;384:1929-1935
2. Broderick JP, Palesch YY, Demchuk AM, Yeatts SD, Khatri P, Hill MD, et al. Endovascular therapy after intravenous t-pa versus t-pa alone for stroke. *The New England journal of medicine*. 2013;368:893-903
3. Tomsick TA, Yeatts SD, Liebeskind DS, Carrozzella J, Foster L, Goyal M, et al. Endovascular revascularization results in ims iii: Intracranial ica and m1 occlusions. *Journal of neurointerventional surgery*. 2014
4. Khatri P, Yeatts SD, Mazighi M, Broderick JP, Liebeskind DS, Demchuk AM, et al. Time to angiographic reperfusion and clinical outcome after acute ischaemic stroke: An analysis of data from the interventional management of stroke (ims iii) phase 3 trial. *The Lancet. Neurology*. 2014;13:567-574
5. Kidwell CS, Jahan R, Saver JL. Endovascular treatment for acute ischemic stroke. *The New England journal of medicine*. 2013;368:2434-2435
6. Ciccone A, Valvassori L, Nichelatti M, Sgoifo A, Ponzio M, Sterzi R, et al. Endovascular treatment for acute ischemic stroke. *The New England journal of medicine*. 2013;368:904-913
7. Qureshi AI, Abd-Allah F, Aleu A, Connors JJ, Hanel RA, Hassan AE, et al. Endovascular treatment for acute ischemic stroke patients: Implications and interpretation of ims iii, mr rescue, and synthesis expansion trials: A report from the working group of international congress of interventional neurology. *Journal of vascular and interventional neurology*. 2014;7:56-75
8. Saver JL, Jahan R, Levy EI, Jovin TG, Baxter B, Nogueira RG, et al. Solitaire flow restoration device versus the merci retriever in patients with acute ischaemic stroke (swift): A randomised, parallel-group, non-inferiority trial. *Lancet*. 2012;380:1241-1249
9. Nogueira RG, Lutsep HL, Gupta R, Jovin TG, Albers GW, Walker GA, et al. Trevo versus merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (trevo 2): A randomised trial. *Lancet*. 2012;380:1231-1240
10. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *The New England journal of medicine*. 2015;372:11-20
11. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *The New England journal of medicine*. 2015
12. Saver JL. Swift prime results. Oral presentation. *Int Stroke Conference*. 2015
13. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *The New England journal of medicine*. 2015
14. Hussain SI, Zaidat OO, Fitzsimmons BF. The penumbra system for mechanical thrombectomy in endovascular acute ischemic stroke therapy. *Neurology*. 2012;79:S135-141
15. Walcott BP, Boehm KM, Stapleton CJ, Mehta BP, Nahed BV, Ogilvy CS. Retrievable stent thrombectomy in the treatment of acute ischemic stroke: Analysis of a revolutionizing treatment technique. *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia*. 2013;20:1346-1349
16. Kuntze Soderqvist A, Kaijser M, Soderman M, Holmin S, Wahlgren N, Andersson T. Mechanical thrombectomy in acute ischemic stroke-experience from 6 years of practice. *Neuroradiology*. 2014;56:477-486
17. Behme D, Gondecki L, Fiethen S, Kowoll A, Mpotsaris A, Weber W. Complications of mechanical thrombectomy for acute ischemic stroke-a retrospective single-center study of 176 consecutive cases. *Neuroradiology*. 2014;56:467-476
18. Nikoubashman O, Reich A, Pjontek R, Jungbluth M, Wiesmann M. Postinterventional subarachnoid haemorrhage after endovascular stroke treatment with stent retrievers. *Neuroradiology*. 2014;56:1087-1096

19. Villwock MR, Singla A, Padalino DJ, Deshaies EM. Acute ischaemic stroke outcomes following mechanical thrombectomy in the elderly versus their younger counterpart: A retrospective cohort study. *BMJ open*. 2014;4:e004480
20. Almekhlafi MA, Davalos A, Bonafe A, Chapot R, Gralla J, Pereira VM, et al. Impact of age and baseline nihss scores on clinical outcomes in the mechanical thrombectomy using solitaire fr in acute ischemic stroke study. *AJNR. American journal of neuroradiology*. 2014;35:1337-1340
21. Brinjikji W, Rabinstein AA, Cloft HJ. Outcomes of endovascular mechanical thrombectomy and intravenous tissue plasminogen activator for the treatment of vertebrobasilar stroke. *Journal of clinical neurology*. 2014;10:17-23
22. Fransen PS. Time to reperfusion and effect of intra-arterial treatment in the mr clean trial. *Int Stroke Conference*. 2015
23. Vagal AS, Khatri P, Broderick JP, Tomsick TA, Yeatts SD, Eckman MH. Time to angiographic reperfusion in acute ischemic stroke: Decision analysis. *Stroke; a journal of cerebral circulation*. 2014;45:3625-3630
24. Kappelhof M, Marquering HA, Berkhemer OA, Majoie CB. Intra-arterial treatment of patients with acute ischemic stroke and internal carotid artery occlusion: A literature review. *Journal of neurointerventional surgery*. 2015;7:8-15
25. Cohen JE, Gomori JM, Rajz G, Itshayek E, Eichel R, Leker RR. Extracranial carotid artery stenting followed by intracranial stent-based thrombectomy for acute tandem occlusive disease. *Journal of neurointerventional surgery*. 2014
26. Maurer CJ, Joachimski F, Berlis A. Two in one: Endovascular treatment of acute tandem occlusions in the anterior circulation. *Clinical neuroradiology*. 2014
27. Lescher S, Czeppan K, Porto L, Singer OC, Berkefeld J. Acute stroke and obstruction of the extracranial carotid artery combined with intracranial tandem occlusion: Results of interventional revascularization. *Cardiovascular and interventional radiology*. 2014
28. Dababneh H, Bashir A, Hussain M, Guerrero WR, Morgan W, Khanna AY, et al. Endovascular treatment of tandem internal carotid and middle cerebral artery occlusions. *Journal of vascular and interventional neurology*. 2014;7:26-31
29. Stampfl S, Ringleb PA, Mohlenbruch M, Hametner C, Herweh C, Pham M, et al. Emergency cervical internal carotid artery stenting in combination with intracranial thrombectomy in acute stroke. *AJNR. American journal of neuroradiology*. 2014;35:741-746
30. Lindsberg PJ, Soinne L, Tatlisumak T, Roine RO, Kallela M, Happola O, et al. Long-term outcome after intravenous thrombolysis of basilar artery occlusion. *Jama*. 2004;292:1862-1866
31. Kumar G, Shahripour RB, Alexandrov AV. Recanalization of acute basilar artery occlusion improves outcomes: A meta-analysis. *Journal of neurointerventional surgery*. 2014
32. Nagel S, Kellert L, Mohlenbruch M, Bosel J, Rohde S, Ringleb P. Improved clinical outcome after acute basilar artery occlusion since the introduction of endovascular thrombectomy devices. *Cerebrovascular diseases*. 2013;36:394-400
33. Mohlenbruch M, Stampfl S, Behrens L, Herweh C, Rohde S, Bendszus M, et al. Mechanical thrombectomy with stent retrievers in acute basilar artery occlusion. *AJNR. American journal of neuroradiology*. 2014;35:959-964
34. Baek JM, Yoon W, Kim SK, Jung MY, Park MS, Kim JT, et al. Acute basilar artery occlusion: Outcome of mechanical thrombectomy with solitaire stent within 8 hours of stroke onset. *AJNR. American journal of neuroradiology*. 2014;35:989-993
35. Broussalis E, Hitzl W, McCoy M, Trinka E, Killer M. Comparison of endovascular treatment versus conservative medical treatment in patients with acute basilar artery occlusion. *Vascular and endovascular surgery*. 2013;47:429-437
36. Mourand I, Machi P, Nogue E, Arquizan C, Costalat V, Picot MC, et al. Diffusion-weighted imaging score of the brain stem: A predictor of outcome in acute basilar artery occlusion treated with the solitaire fr device. *AJNR. American journal of neuroradiology*. 2014;35:1117-1123
37. Andersson T, Kuntze Soderqvist A, Soderman M, Holmin S, Wahlgren N, Kaijser M. Mechanical thrombectomy as the primary treatment for acute basilar artery occlusion: Experience from 5 years of practice. *Journal of neurointerventional surgery*. 2013;5:221-225

38. Fesl G, Holtmannspoetter M, Patzig M, Mayer TE, Pfefferkorn T, Brueckmann H, et al. Mechanical thrombectomy in basilar artery thrombosis: Technical advances and safety in a 10-year experience. *Cardiovascular and interventional radiology*. 2014;37:355-361
39. Lutsep HL, Rymer MM, Nesbit GM. Vertebrobasilar revascularization rates and outcomes in the merci and multi-merci trials. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2008;17:55-57
40. Schonewille WJ, Wijman CA, Michel P, Rueckert CM, Weimar C, Mattle HP, et al. Treatment and outcomes of acute basilar artery occlusion in the basilar artery international cooperation study (basics): A prospective registry study. *The Lancet. Neurology*. 2009;8:724-730
41. McDonald JS, Brinjikji W, Rabinstein AA, Cloft HJ, Lanzino G, Kallmes DF. Conscious sedation versus general anaesthesia during mechanical thrombectomy for stroke: A propensity score analysis. *Journal of neurointerventional surgery*. 2014
42. Takahashi C, Liang CW, Liebeskind DS, Hinman JD. To tube or not to tube? The role of intubation during stroke thrombectomy. *Frontiers in neurology*. 2014;5:170
43. Davis MJ, Menon BK, Baghirzada LB, Campos-Herrera CR, Goyal M, Hill MD, et al. Anesthetic management and outcome in patients during endovascular therapy for acute stroke. *Anesthesiology*. 2012;116:396-405
44. Abou-Chebl A, Lin R, Hussain MS, Jovin TG, Levy EI, Liebeskind DS, et al. Conscious sedation versus general anesthesia during endovascular therapy for acute anterior circulation stroke: Preliminary results from a retrospective, multicenter study. *Stroke; a journal of cerebral circulation*. 2010;41:1175-1179
45. John N, Mitchell P, Dowling R, Yan B. Is general anaesthesia preferable to conscious sedation in the treatment of acute ischaemic stroke with intra-arterial mechanical thrombectomy? A review of the literature. *Neuroradiology*. 2013;55:93-100
46. Berkhemer OA. Impact of general anaesthesia on treatment effect in the mr clean trial. Oral presentation. *Int Stroke Conference*. 2015
47. Talke PO, Sharma D, Heyer EJ, Bergese SD, Blackham KA, Stevens RD. Republished: Society for neuroscience in anesthesiology and critical care expert consensus statement: Anesthetic management of endovascular treatment for acute ischemic stroke. *Stroke; a journal of cerebral circulation*. 2014;45:e138-150
48. Cooray C, Fekete K, Mikulik R, Lees KR, Wahlgren N, Ahmed N. Threshold for nih stroke scale in predicting vessel occlusion and functional outcome after stroke thrombolysis. *International journal of stroke : official journal of the International Stroke Society*. 2015
49. Nedeltchev K, Schwegler B, Haefeli T, Brekenfeld C, Gralla J, Fischer U, et al. Outcome of stroke with mild or rapidly improving symptoms. *Stroke; a journal of cerebral circulation*. 2007;38:2531-2535
50. Heldner MR, Zubler C, Mattle HP, Schroth G, Weck A, Mono ML, et al. National institutes of health stroke scale score and vessel occlusion in 2152 patients with acute ischemic stroke. *Stroke; a journal of cerebral circulation*. 2013;44:1153-1157
51. Spiotta AM, Vargas J, Hawk H, Turner R, Chaudry MI, Battenhouse H, et al. Impact of the aspect scores and distribution on outcome among patients undergoing thrombectomy for acute ischemic stroke. *Journal of neurointerventional surgery*. 2014
52. Daniere F, Lobotesis K, Machi P, Eker O, Mourand I, Riquelme C, et al. Patient selection for stroke endovascular therapy- dwi-aspects thresholds should vary among age groups: Insights from the recost study. *AJNR. American journal of neuroradiology*. 2015;36:32-39
53. Lemmens R, Mlynash M, Straka M, Kemp S, Bammer R, Marks MP, et al. Comparison of the response to endovascular reperfusion in relation to site of arterial occlusion. *Neurology*. 2013;81:614-618
54. Zhu G, Michel P, Aghaebrahim A, Patrie JT, Xin W, Eskandari A, et al. Computed tomography workup of patients suspected of acute ischemic stroke: Perfusion computed tomography adds value compared with clinical evaluation, noncontrast computed tomography, and computed tomography angiogram in terms of predicting outcome. *Stroke; a journal of cerebral circulation*. 2013;44:1049-1055

55. Zhu G, Michel P, Aghaebrahim A, Patrie JT, Xin W, Eskandari A, et al. Prediction of recanalization trumps prediction of tissue fate: The penumbra: A dual-edged sword. *Stroke; a journal of cerebral circulation*. 2013;44:1014-1019

Appendix A:

Strength of evidence supporting recommendations as defined by the Karolinska Stroke Update consensus meeting (1998):

KSU GRADE A evidence: Strong support from randomized controlled trials and statistical reviews (at least one randomized controlled trial plus one statistical review)

KSU GRADE B evidence: Support from randomized controlled trials and statistical reviews (one randomized controlled trial or one statistical review)

KSU GRADE C evidence: No reasonable support from randomized controlled trials, recommendations based on small randomized and/or non-randomized controlled trials evidence.

Appendix B:

Levels and grades of evidence for therapy/prevention as defined by the Oxford centre for evidence-based medicine (2009), resumed:
Grade A: consistent Level 1 studies

Grade B: consistent level 2 or 3 studies or extrapolations from level 1 studies

Grade C: level 4 studies or extrapolations from level 2 or 3 studies

Level 1a: systematic review (homogeneity) of RCTs

Level 1b: individual RCT (with narrow confidence interval)

Level 2a: systematic review (homogeneity) of cohort studies

Level 2b: individual cohort study/low quality RCT e.g. with less than 80% follow-up

Level 3a: systematic review (homogeneity) of case-control studies

Level 3b: individual case-control study

Level 4: case-series

Level 5: expert opinion

Appendix C: Contributors to this Consensus Statement

ESO-Karolinska Stroke Update

Nils Wahlgren, Stockholm, SE (Organiser ESO-Karolinska Stroke Update)

Tiago Moreira, Stockholm, SE (Secretary of the ESO-Karolinska thrombectomy recommendations group)

Olaf Jansen, Kiel, DE (Chair of the interventional committee of the ESNR)

Christophe Cognard, Toulouse, FR (ESMINT and ESNR representative)

Heinrich Mattle, Berne, CH (ESO representative)

Turgut Tatlisumak, Helsinki, FI (ESO representative)

Wim H. van Zwam, Maastricht, NE

Staffan Holmin, Stockholm, SE

Jesper Petersson, Malmö/Lund, SE

ESO representatives

Patrik Michel, Lausanne, CH (Secretary General of ESO)

Valeria Caso, Perugia, IT (President Elect of ESO)

Werner Hacke, Heidelberg, DE

Mikael Mazighi, Paris, FR

Marcel Arnold, Berne, CH

Urs Fischer, Berne, CH

ESMINT and ESNR representatives

Istvan Szikora, Budapest, HU (President of ESMINT)

Laurent Pierot, Reims, FR

Jens Fiehler, Hamburg, DE

Jan Gralla, Berne, CH